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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/525,142	03/14/2000	Pablo Tamayo	2825.1014-001	8330

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EXAMINER

ZHOU, SHUBO

ART UNIT PAPER NUMBER

1631

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/525,142

Applicant(s)

TAMAYO ET AL.

Examiner

Shubo "Joe" Zhou

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 March 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 and 62 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-18, and 62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment and request for reconsideration, filed on 3/22/04, is acknowledged and the amendments entered. Claims 1-18, and the newly added claim 62 are pending and under consideration.
2. The objection of claims 1-18 in the previous Office action is hereby withdrawn in view of applicants' amendment to the claims.

Claim Rejections-35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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5. Claims 1-18, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mack, David H. (US patent no. 6,303,301, date of patent: 10/16/01, filed 5/29/1998), in view of Mangiameli et al. (European J. Operational Research, September 1996, Vol. 93, pages 402-417) .

This rejection is reiterated from the previous Office action.

Mack discloses methods of cluster analysis for gene expression monitoring.

In regard to claim 1, the method by Mack comprises receiving gene expression values of the datapoints, clustering the datapoints, and providing output display indicating the clusters of the datapoints (see Figs 2, 9A and 9B, columns 2, 27-28, especially column 27, lines 48-54). Mack cites the method by Harfigan for such cluster analysis. See column 27. However, Mack does not explicitly disclose clustering using self organizing map (SOM) as required in the instant claims, especially in regard to claims 6-7, and 14-14).

Mangiameli et al. applied SOM and seven hierarchical methods to 252 messy data sets with real-world data imperfections such as dispersion, irrelevant variables, outliers, and nonuniform densities and found that self organizing map is significantly superior in both robustness and accuracy to other clustering methods. See pages 409-416.

The fact that Mangiameli et al. compare SOM and hierarchical clustering method for data analysis indicates that SOM and cluster analysis are art recognized equivalents for the same purpose, i.e. clustering analysis of data. Furthermore, since Mangiameli et al. demonstrates the superiority of SOM in its accuracy and robustness in data analysis, one of ordinary skill in the art

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would have been motivated to modify Mack to use SOM for the analysis of gene expression data.

Further, Mangiameli et al. teaches SOM clustering analysis of data from different sources. See pages 405-409. Thus, there would have been a reasonable expectation of success for modifying Mack and use SOM for the clustering analysis of gene expression data.

In regard to claim 2, the gene expression values are obtained from a gene that is subjected to at least one condition, such as chemical and irradiation treatment (columns 4 and 27).

In regard to claim 3, the step of receiving includes receiving gene expression values of datasets across multiple genes for a condition, such as detection of expression of multiple genes using oligonucleotide array (columns 13-28).

In regard to claim 4, Mack's methods comprising filtering out datapoints to identify genes whose expression is significantly altered (column 2).

In regard to claims 5, 9, 13, and 17, Mack's methods comprise normalizing the value of gene expression using a ratio of the signal for the test samples over the signal of the control probes (see column 17). It would have been well known to an ordinary skill in the art that standard deviation would be used in statistical analysis such as cluster analysis for normalization.

In regard to claims 8, 16, and 62, it would have been obvious to an ordinary person in the art that the amount of outputting/displaying results would vary on the specific needs of individuals. One or more representatives from each cluster could be displayed.

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In regard to claims 10 and 18, it would have been well known in the art that rescaling would often be necessary in a statistical analysis in order to accommodate the vast degree of difference in datasets.

In regard to claims 11 and 12, all the method steps and limitations have been set forth above.

Thus, the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made in view of the combination of the teachings of Mack and Mangiameli et al. et al.

Applicant's arguments, filed 3/22/04, have been fully considered but they are not persuasive.

Applicants' argument is on the ground that none of the cited references teaches clustering gene expression with SOM, and that the combination of the references would produce instead a method of determining causal models using SOM. This is not deemed persuasive. While Mack does use statistical method such as LISREL to produce a causal model, he also teaches using clustering algorithm to analyze the data of gene expression prior to analysis with LISREL. See column 27, lines 48-54. Thus, an embodiment of the Mack's invention is a method of analyzing gene expression data with clustering analysis. Hence, the combination of Mack and Mangiameli et al. would produce, *inter alia*, a method of analyzing gene expression data with SOM.

Applicants further argue that there is no motivation to combine the references because Mack refers to other statistical models when dealing with causal models. This is also not found persuasive. The motivation to combine the references is mainly from Mangiameli et al., who applied SOM and seven hierarchical methods to 252 messy data sets with real-world data imperfections such as dispersion, irrelevant variables, outliers, and nonuniform densities and

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found that self organizing map is significantly superior in both robustness and accuracy to other clustering methods. See pages 409-416. Since Mangiameli et al. demonstrates the superiority of SOM in its accuracy and robustness in data analysis, one of ordinary skill in the art would have been motivated to modify Mack to use SOM instead of the clustering analysis for the analysis of gene expression prior to using LISREL for the causal model analysis.

Conclusion

6. No claim is allowed.
7. THIS ACTION IS MADE FINAL.
8. Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136
(a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization

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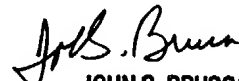
where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst William Phillips whose telephone number is 571-272-0548, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, or on the IFW system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shubo (Joe) Zhou, Ph.D.



Patent Examiner

 28 May 2004
JOHN S. BRUSCA, PH.D.
PRIMARY EXAMINER